

1           3.     The method of Claim 1, wherein the step of analyzing the plurality of images  
2 comprises the steps of generating a plurality of signals, each signal thus generated indicating the  
3 presence of a different discriminable characteristic of the light.

4           4.     The method of Claim 1, wherein the step of analyzing the plurality of images  
5 comprises the step of constructing a sequence library based on each encoded bead that is decoded.

6           5.     The method of Claim 1, further comprising the step of illuminating the plurality of  
7 encoded beads with light while the encoded beads are moving.

8           6.     The method of Claim 1, wherein the step of analyzing the plurality of images  
9 comprises the steps of:

10               (a)     determining dispositions of reporters associated with the bead;

11               (b)     determining a signature of each reporter associated with the bead based upon  
12 the dispositions of the reporters in the plurality of images collected from each encoded bead; and

13               (c)     decoding each bead as a function of each signature associated with the bead.

14           7.     The method of Claim 1, further comprising the step of providing redundant reporters  
15 for each encoded bead.

16           8.     The method of Claim 1, further comprising the step of disregarding the identity of an  
17 encoded bead if the plurality of images for that encoded bead indicate that fewer than a  
18 predetermined number of reporters are associated with the encoded bead.

19           9.     The method of Claim 1, wherein the step of analyzing comprises the step of referring  
20 to an encoded bead legend that identifies each encoded bead as a function of optically discriminable  
21 reporters associated with each encoded bead.

22           10.    The method of Claim 1, further comprising the step of disregarding the identity of  
23 each encoded bead if the analysis of the plurality of images determined that an encoded bead has not  
24 experienced a binding event.

25           11.    The method of Claim 1, wherein the step of analyzing comprises the step of  
26 de-convolving the images if the step of dispersing convolves the plurality of light beams.

27           12.    The method of Claim 1, wherein the step of dispersing comprises the step of providing  
28 an image corresponding to a binding signal produced by the encoded bead.

29           13.    A method for imaging a plurality of encoded beads entrained in a flow of fluid to  
30 identify a compound attached to each encoded bead, corresponding reporters attached to each bead  
31 identifying a unique bead signature, thereby identifying the attached compound, said method  
32 comprising the steps of:

33               (a)     providing an imaging system for imaging encoded beads contained within the  
34 flow of fluid, said imaging system including at least one light source for illuminating an encoded  
35 bead within the flow of fluid passing through the imaging system;

1 (b) focussing light from the encoded bead along a collection path that is in a  
2 direction not aligned with the flow of fluid;

3 (c) dispersing the light that is traveling along the collection path into a plurality of  
4 light beams, as a function of a plurality of different discriminable characteristics of the light, said  
5 plurality of different discriminable characteristics being indicative of an identity of each reporter that  
6 may be attached to the encoded bead;

7 (d) focussing each of the light beams to produce a respective image corresponding  
8 to that light beam;

9 (e) detecting respective images thus produced;

10 (f) generating a plurality of signals based on the respective images, each signal  
11 identifying those reporters present on each encoded bead;

12 (g) analyzing each respective image to determine the identity of each reporter  
13 present on each encoded bead, thereby identifying the compound attached to that bead; and

14 (h) repeating steps (a)-(g) for successive encoded beads in the flow of fluid.

Ar 15 14. The method of Claim 13, wherein the step of analyzing each respective image  
16 comprises the steps of:

17 (a) determining a signature of each reporter associated with the encoded bead  
18 based upon the locations of the reporters on the bead; and

19 (b) identifying the compound as a function of each reporter associated with the  
20 encoded bead.

21 15. The method of Claim 13, wherein the step of analyzing comprises the steps of  
22 disregarding images relating to a reporter if an image from an identical reporter have already been  
23 analyzed, and disregarding all images for an encoded bead if said images indicate that fewer than a  
24 predetermined number of reporters are associated with the encoded bead.

25 16. The method of Claim 13, wherein the step of analyzing comprises the step of referring  
26 to an encoded bead legend that relates each unique set of reporters to a specific compound.

27 17. The method of Claim 16, wherein the step of analyzing comprises the step of  
28 disregarding all images for an encoded bead if it is determined that the encoded bead does not  
29 correspond to said bead legend.

30 18. The method of Claim 13, wherein the step of analyzing comprises the step of  
31 de-convolving the images if the step of dispersing convolves the plurality of light beams.

32 19. The method of Claim 13, wherein the step of dispersing comprises the step of  
33 providing an image corresponding to a binding signal produced by the encoded bead itself.

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1           20.     The method of Claim 19, further comprising the step of disregarding all signals for an  
2 encoded bead if any image relating to that encoded bead indicates that the encoded bead has not  
3 experienced a binding event.

4           21.     A method for simultaneously imaging a plurality of reporters disposed on substantially  
5 different portions of an encoded bead to identify each unique reporter included on the encoded bead,  
6 said method comprising the steps of:

7                   (a)     receiving light from the encoded bead along a plurality of collection paths that  
8 are substantially spaced apart, such that light from the reporters disposed on the different portions of  
9 the encoded bead affect the light received therefrom; and

10                   (b)     processing the light received from the encoded bead along the plurality of  
11 collections paths to identify each unique reporter included on the encoded bead.

12           22.     The method of Claim 21, further comprising the step of providing redundant copies of  
13 each unique reporter on the encoded bead.

Ar 14           23.     The method of Claim 21, further comprising the steps of reducing the number of  
15 unique reporters necessary to encode a bead; and selecting a library to encode a bead characterized by  
16 a length between 9-mer and 16-mer.

17           24.     An imaging system for imaging and decoding a plurality of encoded beads to which is  
18 attached one or more compounds, each compound being associated with a unique reporter set, each  
19 reporter set including at least one reporter, comprising:

20                   (a)     a collection lens disposed so that light traveling from each encoded bead passes  
21 through the collection lens and is focussed along a collection path;

22                   (b)     a dispersing component that receives the light from the collection lens and  
23 disperses the light into a plurality of light beams, as a function of a plurality of different discriminable  
24 characteristics of the light, said plurality of different discriminable characteristics being indicative of  
25 the reporter sets associated with the encoded beads;

26                   (c)     at least one pixilated detector;

27                   (d)     an imaging lens that focuses each of the plurality of light beams on said at least  
28 one pixilated detector, producing a respective image corresponding to each of the plurality of light  
29 beams, said at least one pixilated detector providing an output signal for each respective image, each  
30 output signal indicating the reporter set associated with the encoded bead; and

31                   (e)     a signal processor coupled to receive the output signals from said at least one  
32 pixilated detector, said signal processor processing the output signals to decode each reporter set  
33 associated with the encoded bead, thereby identifying each compound attached to the encoded bead.

34           25.     The imaging system of Claim 24, wherein said signal processor is adapted to  
35 generated sequence contigs from a plurality of decoded beads.

1           26.    The imaging system of Claim 25, wherein said sequence contigs identify at least one  
2 of a genomic DNA sequence, a polymorphic allele, and an expressed gene.

3           27.    The imaging system of Claim 24, wherein said signal processor is adapted to analyze  
4 said output signals to:

5                   (a)    determine dispositions of the reporters on the encoded bead;  
6                   (b)    determine a signature of each reporter associated with the encoded bead based  
7 upon the dispositions of the reporters on the bead; and

8                   (c)    determine a reporter set associated with the encoded bead based upon the  
9 reporter signatures; and

10                  (d)    identify the each compound associated with the reporter set.

11           28.    The imaging system of Claim 24, wherein said signal processor is adapted to disregard  
12 all output signals relating to a reporter if signals from an identical reporter have already been  
13 analyzed, and to disregard all output signals for an encoded bead if said signals indicate that fewer  
14 than a predetermined number of reporters are associated with the encoded bead.

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15           29.    The imaging system of Claim 24, wherein said signal processor is adapted to employ  
16 an encoded bead legend that relates each unique reporter set to a specific compound.

17           30.    The imaging system of Claim 29, wherein said signal processor is adapted to disregard  
18 all output signals for an encoded bead if it is determined that the encoded bead does not correspond to  
19 said encoded bead legend.

20           31.    The imaging system of Claim 24, wherein said signal processor is adapted to  
21 de-convolve the output signals if said dispersing component convolves the plurality of light beams.

22           32.    The imaging system of Claim 24, wherein said dispersing component provides one  
23 respective image corresponding to a binding signal produced by the encoded bead.

24           33.    The imaging system of Claim 32, wherein said signal processor is adapted to disregard  
25 all output signals for an encoded bead if said one respective image indicates that an encoded bead has  
26 not experienced a binding event.

27           34.    The imaging system of Claim 24, wherein said dispersing component comprises one  
28 of a dichroic filters and a prism.

29           35.    The imaging system of Claim 24, wherein said at least one pixilated detector  
30 comprises a time delay integration (TDI) detector.

31           36.    The imaging system of Claim 24, wherein said imaging lens focuses each one of said  
32 plurality of light beams onto a different region of said at least one pixilated detector.

33           37.    A flow imaging system for sequentially imaging and decoding a plurality of encoded  
34 beads entrained in a fluid, said encoded beads comprising one or more compounds from among a  
35 plurality of different compounds, and one or more reporters from among a plurality of different

1 reporters, each different compound being uniquely identified by at least one reporter, said flow  
2 imaging system comprising:

3 (a) at least one light source for illuminating an encoded bead within a flow of fluid  
4 passing through the flow imaging system;

5 (b) a collection lens disposed so that light traveling from an encoded bead passes  
6 through the collection lens and travels along a collection path;

7 (c) a dispersing component that receives the light from the collection lens and  
8 disperses the light into a plurality of light beams, as a function of a plurality of different discriminable  
9 characteristics of the light, said plurality of different discriminable characteristics being indicative of  
10 the plurality of different reporters;

11 (d) at least one pixilated detector;

12 (e) an imaging lens that focuses each of the plurality of light beams on said at least  
13 one pixilated detector, producing a respective image corresponding to each of the plurality of light  
14 beams, said at least one pixilated detector providing an output signal for each respective image, each  
15 output signal identifying those reporters present on the encoded bead; and

16 (f) a signal processor coupled to receive the output signals from said at least one  
17 pixilated detector, said signal processor processing the output signals to decode those compounds  
18 present on the encoded bead, based on the identity of those reporters present on the encoded bead.

19 38. The flow imaging system of Claim 37, wherein said at least one pixilated detector  
20 comprises a time delay and integration (TDI) detector.

21 39. The flow imaging system of Claim 37, wherein said signal processor is adapted to  
22 analyze said output signals to:

23 (a) determine a signature of each reporter associated with the encoded bead based  
24 upon a locations of the reporters on the bead; and

25 (b) identify the compounds as a function of each reporter associated with the  
26 encoded bead.

27 40. The flow imaging system of Claim 37, wherein said signal processor is adapted to  
28 disregard all output signals relating to a reporter if signals from an identical reporter have already  
29 been analyzed, and to disregard all output signals for an encoded bead if said signals indicate that  
30 fewer than a predetermined number of reporters are associated with the encoded bead.

31 41. The flow imaging system of Claim 37, wherein said signal processor is adapted to  
32 de-convolving the output signals if said dispersing component convolves the plurality of light beams.

33 42. The flow imaging system of Claim 37, wherein said dispersing component provides  
34 one respective image corresponding to a binding signal produced by the encoded bead itself.

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1        43. The flow imaging system of Claim 42, wherein said signal processor is adapted to  
2 disregard all output signals for an encoded bead if said one respective image indicates that an  
3 encoded bead has not experienced a binding event.

4        44. A flow imaging system for sequentially imaging and decoding a plurality of encoded  
5 beads entrained in a fluid, said encoded beads comprising one or more compounds from among a  
6 plurality of different compounds, and one or more reporters from among a plurality of different  
7 reporters, each compound being uniquely identified by at least one reporter, said flow imaging  
8 system comprising:

9            (a) a collection lens disposed so that light traveling from an encoded bead passes  
10 through the collection lens and travels along a collection path;

11           (b) a plurality of light reflecting elements disposed in the collection path, each  
12 light reflecting element reflecting light of a different predefined characteristic, and passing light that  
13 does not have that predefined characteristic, the reporters on an encoded bead determining the  
14 characteristics of light traveling along the collection path, each light reflecting element being  
15 positioned at a different location with respect to the collection path to reflect light of a specific  
16 predefined characteristic in a direction different from that of other light reflecting elements, each light  
17 reflecting element being positioned along an axis of said collection path, such that passing light not  
18 reflected by a preceding light reflecting element reaches a last light reflecting element;

19           (c) at least one pixilated detector disposed to receive light that has been reflected  
20 by each of the light reflecting elements, said at least one pixilated detector comprising a plurality of  
21 pixilated regions, each pixilated region producing an output signal that is indicative of at least one  
22 characteristic of the encoded beads and thus indicative of the reporters; and

23           (d) a signal processor coupled to receive the output signals from said the plurality  
24 of regions, said signal processor processing the output signals to decode an identity of the compounds  
25 as a function of the reporters present on the encoded bead.

26        45. The flow imaging system of Claim 44, wherein said plurality of light reflecting  
27 elements comprise dichroic filters.

28        46. A flow imaging system for sequentially imaging and decoding a plurality of encoded  
29 beads entrained in a fluid, said encoded beads comprising one or more compounds from among a  
30 plurality of different compounds, and one or more reporters from among a plurality of different  
31 reporters, each compound being uniquely identified by at least one reporter, said flow imaging  
32 system comprising:

33           (a) a collection lens disposed so that light traveling from an encoded bead object  
34 passes through the collection lens and travels along a collection path;

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1 (b) a dispersing component that receives the light from the collection lens and  
2 disperses the light into a plurality of light beams, as a function of a plurality of different discriminable  
3 characteristics of the light, said plurality of different discriminable characteristics being indicative of  
4 the plurality of different reporters;

5 (c) a plurality of light sensitive regions disposed on at least one detector;

6 (d) an imaging lens that focuses each of the plurality of light beams on said  
7 plurality of light sensitive regions, producing a respective image corresponding to each of the  
8 plurality of light beams, said plurality of light sensitive regions providing an output signal for each  
9 respective image, each output signal indicating those reporters present on the encoded bead; and

10 (e) means for processing the output signals to decode a sequence of the plurality of  
11 components.

12 47. The flow imaging system of Claim 46, wherein said means comprise a signal  
13 processor coupled to receive the output signals from said at plurality of regions.

Ar 14 48. The flow imaging system of Claim 46, wherein said means decodes a sequence of the  
15 plurality of components by:

16 (a) determining dispositions of the reporters on the encoded bead;

17 (b) determining a signature of each reporter associated with the encoded bead  
18 based upon the dispositions of the reporters on the bead; and

19 (c) identifying each compound as a function of each reporter associated with the  
20 encoded bead.

21 49. The flow imaging system of Claim 46, wherein said means disregards all output  
22 signals relating to a reporter if signals from an identical reporter have already been analyzed for the  
23 encoded bead, and disregards all output signals for an encoded bead if said signals indicate that fewer  
24 than a predetermined number of reporters are associated with the encoded bead.

25 50. The flow imaging system of Claim 46, wherein said means de-convolves the output  
26 signals if said dispersing component convolves the plurality of light beams.

27 51. A flow imaging system for sequentially imaging and decoding a plurality of encoded  
28 beads entrained in a fluid, said encoded beads being associated with one or more compounds from  
29 among a plurality of different compounds, and with one or more reporters from among a plurality of  
30 different reporters, each compound being uniquely identified by at least one reporter, said flow  
31 imaging system comprising:

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1 (a) a fluid system comprising an unanalyzed encoded bead supply, a detection  
2 volume, and an analyzed encoded bead reservoir, said fluid system being specifically adapted to  
3 hydrodynamically focus fluid moving from said unanalyzed encoded bead supply into said detection  
4 volume, such that encoded beads pass through said detection volume one at a time and into the  
5 encoded bead reservoir;

6 (b) means for collecting image data from each encoded bead passing through said  
7 detection volume, said image data being indicative of at least one characteristic of the encoded bead  
8 passing through the detection volume that is determinative of the reporters associated with the encoded  
9 bead; and

10 (c) a signal processor capable of decoding a plurality of encoded beads based on  
11 said at least one characteristic of the encoded beads collected by said means, to determine the compounds  
12 associated with each encoded bead that has been analyzed.

13 52. The flow imaging system of Claim 51, wherein said means for collecting image data  
14 from each encoded bead comprises:

15 (a) a collection lens disposed so that light traveling from the encoded beads passes  
16 through the collection lens and travels along a collection path;

17 (b) a dispersing component that receives the light from the collection lens and  
18 disperses the light into a plurality of light beams, as a function of a plurality of different discriminable  
19 characteristics of the light, said plurality of different discriminable characteristics being indicative of  
20 the plurality of different reporters;

21 (c) at least one pixilated detector;

22 (d) an imaging lens that focuses each of the plurality of light beams on said at least  
23 one pixilated detector, producing a respective image corresponding to each of the plurality of light  
24 beams, said at least one pixilated detector providing an output signal for each respective image, each  
25 output signal indicating those reporters present on the encoded bead; and

26 (e) a signal processor coupled to receive the output signals from said at least  
27 plurality of pixilated detectors, said signal processor processing the output signals to decode an  
28 identity of the compounds associated with each encoded bead analyzed.

29 53. The flow imaging system of Claim 51, wherein said signal processor is adapted to  
30 analyze said output signals to:

31 (a) determine locations of the reporters on the encoded bead,

32 (b) determine a signature of each reporter associated with the encoded bead based  
33 upon the locations of the reporters on the bead; and

34 (c) identify the compounds associated with each encoded bead as a function of  
35 each reporter associated with each encoded bead analyzed.



1        54. The flow imaging system of Claim 51, wherein said signal processor is adapted to  
2 disregard all output signals relating to a reporter if signals from an identical reporter have already  
3 been analyzed, and to disregard all output signals for an encoded bead if said signals indicate that  
4 fewer than a predetermined number of reporters are associated with the encoded bead.

5        55. The flow imaging system of Claim 51, wherein said signal processor is adapted to  
6 de-convolving the output signals if said dispersing component convolves the plurality of light beams.

7        56. The flow imaging system of Claim 51, wherein said dispersing component provides  
8 one respective image corresponding to a binding signal produced by the encoded bead itself.

9        57. The flow imaging system of Claim 56, wherein said signal processor is adapted to  
10 disregard all output signals for an encoded bead if said one respective image indicates that an  
11 encoded bead has not experienced a binding event.

12        58. A method of employing an oligo library encoded on beads for at least one of a DNA  
13 sequencing, a polymorphism analysis, and an expression analysis, said method comprising the steps  
14 of:

15                (a) providing an imaging system capable of decoding a sequence of encoded beads  
16 conveyed in a flow of fluid;

17                (b) generating a complete encoded bead library of N-mer oligos;

18                (c) selectively performing one of said DNA sequencing, said polymorphism  
19 analysis, and said expression analysis based on imaging data produced by imaging the encoded beads  
20 with the imaging system;

21                (d) when the DNA sequencing is selected, amplifying genomic DNA using  
22 primers for extended sequences of interest;

23                (e) when the polymorphism analysis is selected, amplifying genomic DNA using  
24 primers for polymorphic regions of interest;

25                (f) when the expression analysis is selected, amplifying RNA using primers for  
26 genes of interest;

27                (g) hybridizing an amplified component produced by any of steps (d)-(f) in  
28 relationship to said encoded bead library;

29                (h) analyzing the encoded beads using the imaging data to identify oligo sequences  
30 of encoded beads hybridized in step (g); and

31                (i) constructing sequence contigs from the oligo sequences identified in step (h) to  
32 identify one of a genomic DNA sequence, a polymorphic allele, and an expressed gene.

33        59. The method of Claim 58, wherein said N-mer oligos comprises oligos having a length  
34 equal to ten.--

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